Table 7-3: Updated findings of feasible alternatives to ODS in analytical procedures

ODS	Methodology		Feasible Substitutes	
ODS Type	General use	Methodology	Substance / Methodology	Methodology
CCl4	Standard method	Analysis of Cyanocobalamin, United States Pharmacopea (USP) Method.	Coulometric electrochemical and ultraviolet detection	Determination of cyanocobalamin, betamethasone, and diclofenac sodium in pharmaceutical formulations, by high performance liquid chromatography. L. González, G. Yuln and M. G. Volonté High-performance liquid chromatography method for the simultaneous determination of thiamine hydrochloride, pyridoxine hydrochloride and cyanocobalamin in pharmaceutical formulations using coulometric electrochemical and ultraviolet detection. Marcin Leszek Marszałł, Anna Lebiedzińska, Wojciech Czarnowski and Piotr Szefer.
CCl4	Standard Method	Analysis of cascarosides	- Dichloro methane, - Chloroform Ttrichloroethylene	
CCl4	Standard Method	Analysis of simethicone by Infrared spectroscopy / Cleaning of IR cells (Valuation of Simethicone in finished products, using infrared spectroscopy (IR). Method "Simethicone Capsules" of Official Monographs USP XXIV (p. 1519).)	Chloroform Toluene	ICP-AES Determination of Trace Simethicone Levels in Biopharmaceutical Products. J. Qiu, V. Wong, H. Lee, C. Zhou J Pharm Biomed Anal. 2002 Sep 5;30 (2):273-8 12191712. A RP-LC method with evaporative light scattering detection for the assay of simethicone in pharmaceutical formulations. Douglas E Moore, Tina X Liu, William G Miao, Alison Edwards, Russell Elliss. Faculty of Pharmacy, The University of Sydney, Sydney 2006, Australia.
CCl4	Standard Method	Analysis of Trimethoprim. United States Pharmacopea (USP) Method (Also at: S.Z. Qureshi; M.I.H Helaleh; N. Rahman; R.M.A.Q. Jamhour; "Spectrometric determination of trimethoprim by oxidation in drugs formulations; Fresenius J Anal Chem (1997) 357: 1005-1007; Springer-Verlag 1997)	- Acetonitrile and methanol	L. K. Sørensen&, T. H. Elbæk; "Simultaneous Determination of Trimethoprim, Sulfadiazine, Florfenicol and Oxolinic Acid in Surface Water by Liquid Chromatography Tandem Mass Spectrometry"; Chromatographia **2004**, 60, September (No. 5/6); p. 287.
CCl4	General Method	Analysis of conjugated estrogens by gas chromatography		No alternatives found.
CCl4	Standard Method	Analysis of Furazolidone, United States Pharmacopea (USP) Method	- UV detection	S. M. Hassan / F. A. Ibrahim* / M. S. El-Din / M. M. Hefnawy; "A Stability-Indicating High-Performance Liquid Chromatographic Assay for the Determination of Some Pharmaceutically Important Nitrocompounds"; Chromatographia

ODS	Methodology		Feasible Substitutes	
				Vol. 30, No. 3/4, August 1990; p. 176.
CCl4	General method	Analysis of copper gluconate	Dichloromethane, - Chloroform -Trichloro-ethylene	
CCl4	Standard Method	Gravimetric determination of sulfur, Collaborative International Pesticides Analytical Council CIPAC Method [1]	- Gravimetric method	Gravimetric method using nitric acid. Reflux with ethanol and titration with iodine, according to CIPAC (Collaborative International Pesticides Analytical Council Limited)
CCl4	Standard Method	Determination of specific weight in cement samples (National standard NCh 154 Of. 69 / ASTM C 243-95, Standard test)	- Kerosene Benzene	ASTM C 188-44 (Revised in 1967)
CCl4	Standard Method	ASTM D 2821-96[2], Standard Test Method for Measuring the Relative Stiffness of Leather by Means of a Torsional Wire Apparatus	Trichloroethylene	
CCl4	Standard Method	ASTM D 3921-85 (re-approved in 1990), Standard test method for oil and grease and petroleum hydrocarbons in water	- Perchloroethylene	ASTM D7066-04
CCl4	Standard Method	Determination of hydrocarbons in water ASTM D3921-96 / D3921-97	- Perchloroethylene S-316 (dimer/trimer of chlorotrifluoro ethylene)	
CCl4	Standard Method	Determination of the jellification point. Method M SAC 10 14 11 (Own method)		No alternatives found
CCl4	Standard Method	Iodine index by volumetry in oil and greases AOCS CD 1-25 "Iodine Value (Wijs)"	- Hexane Cyclohexane and acetic acid Chloroform Iso-octane	Method CD1D-92
CCl4	Standard method	Iodine[3] index by ASTM D1959-97 Standard Test Method for Iodine Value of Drying Oils and Fatty Acids (Withdrawn 2006) ASTM D5554- 95 (2006) Standard Test Method for Determination of the Iodine Value of Fats and Oils.	Cyclohexane and acetic acid and diluted with iodine monobromide solution.	[4] Hanus ISO 3961:1996

[1] Note: The sulphur is converted by refluxing with sodium sulphite to sodium thiosulphate. The thiosulphate is then titrated with Standard iodine solution. CIPAC Handbook E.

[2] Updated by ASTM D2821-00(2005)e1.

[3] The Iodine value expresses the content of compounds with unsaturated carbon-carbon double bonds. It is determined by adding a halogen, e.g. iodine to the simple.

ODS	Methodology		Feasible Substitutes	
CCl4	General Method	Liquid-liquid partitioning method, for iodide and bromide analysis	- Dichloromethane. Chloroform	
CCl4	Standard Method	Extraction of iodine and its derivatives and thyroid extracts from semi-solid pharmaceutical preparation. United States Pharmacopea (USP) method	- Petroleum ether Hexane Chloroform Dichloromethane Benzene Hexane + ethyl acetate	
TCA	Standard Method	Bromine index ASTM D2710-99 Determination of bromine number ASTM ASTM D1159-07[5]	- Dichloromethane Diethylcarbonate 1-methyl-2-pirrolidone Dichloro-methane	ASTM D 2710[6] ASTM D 1159-07
CCl4	General Method	Determination of copper	- Chloroform Dichloromethane Perchloroethylene Trichloroethylene	Flame Atomic Absorption Spectrometric Methods Research and Development (2) Page 25.
CCl4	General Method	Arsenic extraction	- Chloroform	Atomic Absorption Spectrometry AAE with hydride generation
CCl4	General Method	Analysis of chloride in saline solutions	- Aliphatic hydrocarbon Chloroform Dichloromethane Perchloroethyle	

[4] In the determination of the iodine value according to Hanus the sample is dissolved in cyclohexane and acetic acid and diluted with iodine monobromide solution. Potassium iodide and water are added, and the formed iodine is titrated back with sodium thiosulphate solution. The methods according to Wijs and Kauffmann slightly differ from the Hanus method. Information on the accuracy of the methods is given in the test methods. Only in the case of some oils with a high iodine value can the results deviate from one another. Cyclohexane and acetic acid have generally substituted chloroform (trichloromethane, not an ozone depleting substance) and carbon tetrachloride. Also ISO 3961:1996, which is similar to the Wijs method, uses cyclohexane and acetic acid. The modified Hofmann and Green method allows a shorter reaction time, and is recommended for samples containing hydroxy fatty acids because the substitute reactions occurring in this case using the Wijs method do not take place. (Ref. TemaNord 2003:516)

[5] ASTM D 1159 is generally applicable for gasoline, kerosene and distillates in the gas oil range that fall in specific distillation and bromine number limits. However, the method is not satisfactory for normal alpha-olefins. The method can be used to estimate the percentage of olefins in petroleum distillates boiling up to approximately 315ºC by using a calculation method described in the standard. Dichloromethane is temporarily being allowed as an alternative to 1,1,1-trichloroethane (an ozone depleting substance) until a permanent substitute can be identified and adopted by ASTM. A program to identify and evaluate candidate solvents is currently underway in the Subcommittee D02.04. (Ref. TemaNord 2003:516; “Use of ozone depleting substances in laboratories”; © Nordic Council of Ministers, Copenhagen 2003 ISBN 92-893-0884-2).

[6] This method also mentioned dichloromethane as an alternative to TCA.

ODS	Methodology		Feasible Substitutes	
			ne. In the first cleaning stage: benzene / ether.	
CCl4	Solvent	Washing of NMR (Nuclear Magnetic Resonance) tubes	- Acetone	Washing should be followed by oven-drying of inverted tubes to remove traces of acetone.
CCl4	Solvent	Grease solvent and cleaning of glass materials	- Acetone	A chlorinated solvent such as chloroform, trichloroethylene or dichloromethane may also be used.
CCl4	Solvent	Organic synthesis	- Dichloromethane Chloroform	
CCl4	Carrier (inert); analytical equipmet (Infrared)	Reaction of phenol and aromatics. Oxygen containing functional groups - Noncarbonyl Groups, Example: The determination of hydroxyl values of alcohols, page 34.	- Perchloroethylene	Welcher 6th Edition, p. 1180.[7]
CCl4	Carrier, analytical use.	Solvent in metals analysis by UV-Vis spectrometry, with ditizone (International method). / "Titration of cadmium: Photometric Method with Ditizone", page 44.	- Chloroform Dichloromethane Benzene Toluene Cadmium sulfide can be extracted from solution with iodine	Furman Sixth Edtion pp. 254-256[8]
CCl4	Solvent	Solvent of polymers	- Tetrahydrofurane. Chloroform. Dichloromethane. Dichloro-ethane	
CCl4	Carrier (inert); analytical equipmet - Infrared analysis for spectral range 4000 to 50 cm-1	Spectrophotometry IR (USP XXIII) "Standard practice for general techniques for qualitative infrared analysis E 1252-94", page 26	- Toluene Carbon disulphide	[9]

[7] Research and Development (ICE Consulting, "Consumption of Ozone Depleting Substances (ODS) by Laboratories in the European Community and ODS-Free Methods to Reduce Further ODS Use - Confidential Report Prepared for the European Commission - April 2005".

[8] Research and Development (ICE Consulting, "Consumption of Ozone Depleting Substances (ODS) by Laboratories in the European Community and ODS-Free Methods to Reduce Further ODS Use - Confidential Report Prepared for the European Commission - April 2005".

[9] Research and Development (ICE Consulting, "Consumption of Ozone Depleting Substances (ODS) by Laboratories in the European Community and ODS-Free Methods to Reduce Further ODS Use - Confidential Report Prepared for the European Commission - April 2005".

ODS	Methodology		Feasible Substitutes	
CFC-113	Standard Method	US EPA Office of Water Method 418.1, extraction of total petroleum hydrocarbons from water samples, for analysis by infrared spectroscopy "Petroleum Hydrocarbons, Total Recoverable - Spectrometric, Infrared"	- S-316 (dimer/trimer of chlorotrifluoroethylene	ASTM D 7066-04 "Test Method for dimer/trimer of Chlorotrifluoroethylene S-316 recoverable oil and grease and non polar material by infrared determination".
CCl4	Carrier (inert), analytical equipment, GC	Adsorption Chromatography (Welcher 6th edition pp 216-219,[10] page 38.	- Petroleum ether Cyclohexane Carbon disulfide Diethyl ether Benzene Esters Chloroform Dichloroethane Alcohols Water Pyridine Organic acid Inorganic acids and bases.	Welcher Sixth Edition pp. 216-219.
CCl4	Vapor producer	Test of breakthrough times of gas mask cartridges and canisters in the National Approval Test of Respirators. Testing of breathing filters (personal safety equipment), 42 CFR part 84	- Cyclohexane	Mitsuya FURUSE1, Seiichiro KANNO, Tsuguo TAKANO and Yoshimi MATSU; "Cyclohexane as an Alternative Vapor of Carbon Tetrachloride for the Assessment of Gas Removing Capacities of Gas Masks"; National Institute of Industrial Health, Kawasaki, Japan; Industrial Health 2001, 39, 1–7.
CCl4	Solvent	*O*- and *N*- difluoromethylations	- Chlorodifluoromethyl phenyl sulfone	Ji Zhenga, Ya Lia, Laijun Zhanga, Jinbo Hu*.a, Gerrit Joost Meuzelaarb, and Hans-Jürgen; "Chlorodifluoromethyl phenyl sulfone: a novel non-ODS based difluorocarbene reagent for *O*- and *N*-difluoromethylations"; Supplementary Material (ESI) for Chemical Communications. This journal is © The Royal Society of Chemistry 2007.

7.4.2 Case studies

Some case studies were also developed to explore how the restrictions on the use of one ODS, carbon tetrachloride (CTC) for laboratory and analytical purposes were implemented in some jurisdictions.

Australia

A bottom-up investigation of the use of carbon tetrachloride (CTC) in research laboratories in Australia was undertaken.

[10] Research and Development (ICE Consulting, "Consumption of Ozone Depleting Substances (ODS) by Laboratories in the European Community and ODS-Free Methods to Reduce Further ODS Use - Confidential Report Prepared for the European Commission - April 2005".